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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,294	12/28/2001	Jean Marie Vogel	9676-311	2836

20582 7590 08/23/2005

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,294	VOGEL ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-16,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-16,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response, Applicant's Arguments/Remarks and the request for extension of time (3 months-granted), all filed 06/10/05 is acknowledged.

Claims 1-4, 8-16 and 19-20 are pending. No amendment to the claims has been made. Claims 1-4, 8-16 and 19-20 remain rejected.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-4, 8-16, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rajagopalan *et al.* (US Pat. No. 5,843,987) in view of Boschetti *et al.* (US Pat. No. 5,635,215).

Rajagopalan teaches a method for treating gastroesophageal reflux disease (GERD), which comprises parenterally administering particles of ellagic acid, which is known to be useful for the treatment of gastrointestinal disorders, such as GERD, to a human or other animal (see reference column 1, lines 1-18); (col. 2, lines 21-57); (col. 5, lines 15-42); examples and claims.

According to Rajagopalan, ellagic acid has prokinetic activity, and therefore stimulates motility of the gastrointestinal tract, enhances esophageal contractility, gastric emptying and small intestine transit time. Furthermore, ellagic acid is useful in the treatment of constipation,

heartburn, non-ulcer esophagitis, GERD, esophagitis, gastric ulcers, and/or duodenal ulcers (col. 2, lines 25-35).

The method of treatment can be accomplished by administration of ellagic acid in various suitable unitary dosage forms, such as orally, parenterally, or rectally. Oral liquid dosage forms include suspensions, syrups, elixirs and solutions. Solid dosage forms include powders, pills, compressed tablets, hard capsules containing beads or particles of ellagic acid or soft gelatin capsules. Oral dosage forms can also be film coated. For parenteral dosage forms, acceptable carriers include sterile water, saline solution, glucose solution or mixtures of saline and glucose solutions (col. 5, lines 26-42).

The examples at columns 10-12 demonstrate various dosage forms, such as oral solutions, suspensions and parenteral solutions. Example 5 demonstrates the teaching of a parenteral solution of ellagic acid in combination with propylene glycol, chlorocresol and water for injection.

What is lacking in Rajagopalan is collagen (or a derivative thereof) or glucosaminoglycans as the particular coating material of the microparticles.

Boschetti ('215) teaches microspheres and injectable solutions comprising a hydrophilic copolymer coated with a cell adhesion promoter, wherein different types of cell adhesion promoters, include, collagen, gelatin, glucosaminoglycans, lectins, polycations, or any other synthetic biological cell adhesion agent and wherein the presence of a cationic charge on the surface of the microspheres makes it possible to initiate and improve cell adhesion (see reference column 1, line 46 through col. 2, line 42).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use hydrophilic copolymer coatings, that are coated with cell adhesion agents (*i.e.*, collagen, glucosaminoglycans) as taught by Boschetti with the injectable particles of Rajagopalan because Boschetti teaches that the microspheres hydrophilic character enables them to be placed in suspension, without formation of aggregates nor adhesion to the walls of the catheters, syringes, needles and other materials used in embolization and similarly Rajagopalan teaches parenteral administration of particles, specifically of ellagic acid for the treatment of gastrointestinal reflux disease. The expected result would be a hydrophilic-coated formulation comprising injectable particles for the treatment of various gastrointestinal disorders.

Regarding the administration of the microparticles into the walls of the lower esophageal sphincter or the diaphragm, the prior art (Rajagopalan) teaches parenteral administration of particles into the gastrointestinal tract. The gastrointestinal tract as used therein, includes the entire digestive tract, including the esophagus, stomach, small intestine, large intestine, and the colon (see col. 4, lines 64-67). One of ordinary skill in the pharmaceutical art could determine a suitable means and route of administration based on the intended locality of treatment. There is no criticality seen in the particular localized area of administration, (*i.e.* walls of esophageal sphincter) since the prior art teaches the administration of particles into the gastrointestinal tract for the treatment of gastro-related diseases, such as GERD and thus this would include all areas of the esophageal sphincter or diaphragm, including the walls.

Response to Arguments

Applicant's arguments filed 06/10/05 have been fully considered but they are not persuasive.

Applicant argued regarding the rejection of Claims 1-4, 8-16, 19 and 20 over Rajagopalan et al. (US '987) in view of Boschetti et al. (US '215) stating, "There is nothing in the cited art that would suggest to those of ordinary skill in the art that they should treat GERD by administering Rajagopalan's ellagic acid compositions directly to the lower esophageal sphincter or diaphragm, thereby effecting tissue bulking at those sites, that it would have a reasonable expectation of actually working. Rajagopalan's formulations are designed to disintegrate in the GI tract, thereby releasing ellagic acid, the active ingredient in the tract. Rajaopalan's formulations would therefore not effect tissue bulking in the GI tract, let alone specifically the lower esophageal sphincter or diaphragm. There is nothing in the cited art that would suggest to those of ordinary skill in the art to coat Rajagopalan's formulations with collagen, pursuant to the teachings of Boschetti. Boschetti discloses a microsphere comprising a hydrophilic acrylic copolymer that may be coated with a cell adhesion promoter, uses those microspheres for embolization, i.e., vascular occlusion. Occluding vessels involve different considerations and techniques than those involved in tissue bulking for the treatment of GERD. While the microspheres that Boschetti uses may be coated with a cell adhesion promoter, Rajagopalan's formulations are not suited for coating with cell adhesion promoters, such as collagen. Coating Rajagopalan's formulations with anything would contravene the purpose of

Rajaopalan's formulations, which is to deliver ellagic acid to the GI tract, thereby treating GERD. Rajagopalan's formulations would not effect tissue bulking in the GI tract with or without a coating of collagen, let alone specifically the lower esophageal sphincter or diaphragm. Rajagopalan actually teaches away from the present invention. Applicants submit that the rejection of the claims over Rajagopalan and Boschetti is based on the use of impermissible hindsight."

These arguments have been fully considered, but were not found to be persuasive. The prior art teaches a similar method of treatment for the same disease as instantly claimed, gastroesophageal reflux disease or GERD. Applicant's argument that 'Rajaopalan's formulations would not effect tissue bulking in the GI tract, let alone specifically the lower esophageal sphincter or diaphragm' is not persuasive since the prior art teaches and recognizes parenteral administration of hydrophilic microparticles for treating GERD. Applicants have not demonstrated any surprising or unexpected results, which accrue from the administration of particles being into the lower esophageal sphincter or diaphragm. Moreover, with regards to 'tissue-bulking amounts', as presently claimed, it is noted that the generic claim is silent as to any preferred tissue-bulking amounts. The term appears to be a functional expression with no specific units disclosed for the generic claim. Applicants have also not demonstrated that the amounts taught by the prior art are not tissue-bulking amounts. The Examiner notes that the prior art also teaches suitable and effective amounts of ellagic acid to treat gastrointestinal disorders. Dosage ranges are generally from about 1 mg to about 300 mg of ellagic acid daily (see col. 3, lines 5-10). Boschetti was cited for the teaching of the obviousness of employing microspheres and injectable solutions whereby the hydrophilic particles are coated with cell

adhesion promoters (i.e., collagen, glucosaminoglycans), such as instantly claimed. Applicant's specification, at page 17, lines 10-16, disclose that "microparticles of the present invention which have the specific properties of cell adhesion and growth promotion can be used directly for tissue bulking." Ample motivation is provided by the prior art to incorporate hydrophilic copolymer coatings, that are coated with cell adhesion agents (*i.e.*, collagen, glucosaminoglycans) as taught by Boschetti within the formulation of Rajagopalan because Boschetti teaches that the microspheres hydrophilic character enables them to be placed in suspension, without formation of aggregates nor adhesion to the walls of the catheters, syringes, needles and other materials used in embolization. The combined prior art teachings provide for a similar method for administering microparticles, used to treat the same disease, to the same patient population, and for the same intended purpose as that claimed by Applicant.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Therefore, since, the prior art combinations provide for similar administration methods for treating the same disease (GERD), used for the same purpose as the applicants, a *prima facie* case of obviousness has been established.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday through Friday from 8:00A.M. to 5:30P.M., alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

H. N. Sheikh H.N.S.

Patent Examiner

Art Unit 1615

August 12, 2005

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER